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THE USE OF HYPOTHERMIA IN THE PREVENTION OF BRAIN DAMAGE FOLLOWING TEMPORARY ARREST OF CEREBRAL CIRCULATION: EXPERIMENTAL OBSERVATIONS*

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Recent developments in arterial surgery directed toward excision of diseased segments and their replacement with homografts have provided a much more favorable outlook for these conditions. There are, however, certain limitations to the application of this form of therapy, one of the most important of which arises from the technical necessity of arresting circulation during performance of the procedure. As a consequence of this temporary interruption of blood flow, serious ischemic damage to the tissues distal to the point of occlusion may take place depending upon a number of factors, including particularly the period of occlusion and the sensitivity of the tissues to anoxia. The tissues of certain vital organs, for example, such as those of the central nervous system, are highly vulnerable to damage from temporary ischemia and even relatively short periods of interruption of blood flow to these tissues may produce grave neurologic disturbances. This problem thus assumes particular importance in the application of excisional therapy for lesions involving arteries such as those about the aortic arch that supply such vital organs.

One approach to this problem that seems promising is through the use of hypothermia and the consequent reduction of oxygen demand by the tissues of the central nervous system.[2] Previous studies have shown that hypothermia has a definite protective influence against ischemic damage of the spinal cord following high aortic occlusion.[1, 9] Accordingly these studies were undertaken to determine the effectiveness of hypothermia in preventing cerebral damage following temporary arrest of the cerebral circulation in the dog.

Extirpation of the common or internal carotid artery in man may be expected to result in a mortality of 40 to 50 per cent.[7] In lower animals,

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however, such a procedure is followed by minimal disturbance, owing to the presence of extensive collateral circulation through the vertebral and accessory pathways.[5] For these reasons much of our experimental work was directed toward the development of a suitable preparation which would produce neurologic sequelae in a substantial number of cases as controls.

METHOD

Mongrel dogs ranging from 7 to 14 kilograms in weight were used in all the experiments. Anesthesia was obtained by intravenous Nembutal, 30 mg. per kilogram of body weight, and artificial respiration was provided by

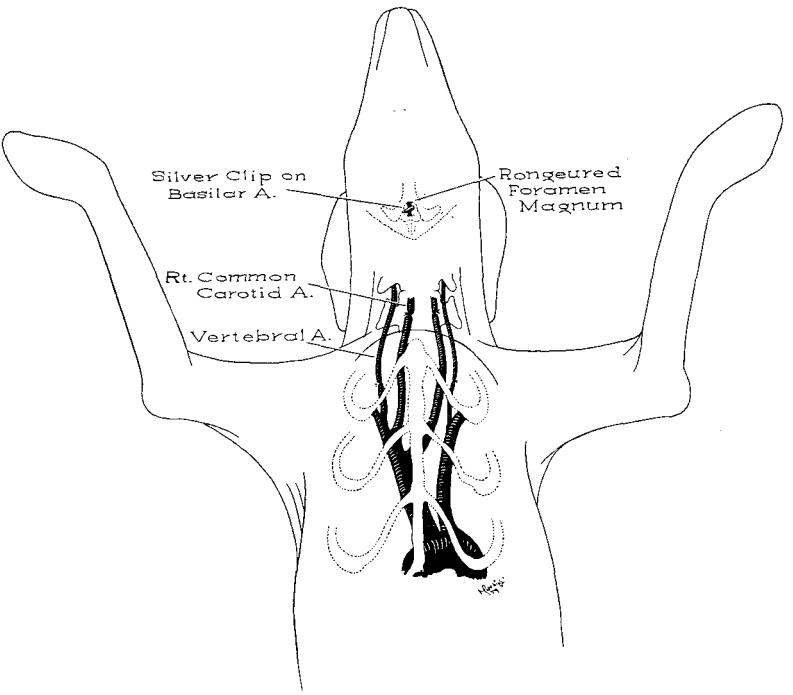

Fig. 1. Diagrammatic representation of points of occlusion.

means of endotracheal tube and mechanical insufflator. Preliminary observations in 30 dogs revealed no detectable neurologic changes following periods of occlusion up to one hour of the brachiocephalic, subclavian, carotid and vertebral arteries in various combinations. It thus became apparent that further impediment to cerebral blood flow was necessary. Accordingly the following experiments were performed:

Group I. A permanent silver clip was placed upon the basilar artery and a tourniquet applied around the neck. The basilar artery was approached anteriorly through the foramen magnum with the structures of the neck retracted laterally, and the anterior portion of the occipital bone was carefully ronguered away for exposure. The dura was transversed to apply the clip. The tourniquet about the neck was occluded for 30 minutes at a pressure of 900 mm. Hg.

Group II. In addition to the procedure employed in group I, the carotid and vertebral arteries were temporarily occluded at the root of the neck for

a similar period of time to reduce deep circulation not affected by the tourniquet (Fig. 1).

Group III. The procedure used on these animals was the same as that done for those in group II but in addition a state of hypothermia was induced with rectal temperature ranging from 25° to 31° C. during the period of occlusion. Hypothermia was produced by wrapping the animals in a rubberized blanket through which a refrigerant solution was circulated. Following completion of the experiment rewarming was accomplished with the same blanket through which hot water was circulated.

RESULTS

In group I five of the six dogs made spontaneous recovery with no apparent neurologic disturbances (Table 1). The sixth animal, however, developed a dilated pupil during occlusion and, although recovering from anesthesia, died with generalized convulsions which were set off by auditory or tactile stimuli.

Table 1. Results Following Temporary Occlusion of Cerebral Circulation

EXPERIMENTS	NUMBER OF ANIMALS	RECOVERED	DIED	
			NUMBER	PER CENT
Group I	6	5	1	16.7
Group II	9	3	6	66.6
Group III	9	9	0	0

In group II three of the nine dogs made eventual complete recovery (Table 1). Of these, two resumed respirations promptly while the third required artificial respiration for 8 hours. All of the fatal group developed a dilated pupil within 3 to 9 minutes after occlusion. Three of these failed to resume respiration in from 2 to 6 hours. Although respiration returned in two of the others, they subsequently developed convulsions and died in 24 hours. The remaining animal died in 6 hours without convulsions.

In group III all of the nine animals treated with hypothermia recovered and none developed a dilated pupil (Table 1). All were observed for a period of a month with no obvious neurologic changes.

The significantly greater morbidity and mortality in group II as compared with group I would seem to be related to the increased degree of diminution of cerebral circulation. The striking difference in the mortality between group II and group III would appear to be due to the use of hypothermia in the latter as this was the only difference in these experiments.

DISCUSSION

Previous investigations along these lines have indicated the usefulness of hypothermia in preventing ischemic damage to the spinal cord following temporary arrest of the circulation in the aorta.[1, 9] Thus the incidence of paraplegia and death following high aortic occlusion, just distal to the left subclavian, for one hour was reduced from 76 per cent in a group of 50 control animals to 25 per cent in a group of 47 hypothermic animals.[9] Even more striking, however, was the reduction in the paraplegic ratio among the surviving animals in the two groups, the figures being 65 per cent for the 34 control animals and 0 per cent for the 35 hypothermic animals. Clini-

cally there is also reason to believe that hypothermia may have protective value in preventing ischemic cord damage following temporary cross-clamping of the thoracic aorta. The threat of this complication has been demonstrated following such a procedure in the treatment of extensive aneurysms of the thoracic aorta.[3, 6] In an effort to reduce this hazard hypothermia has been employed in 6 cases of aneurysms of the thoracic aorta arising in the distal part of the arch in which resection with homograft replacement was done.[4] In spite of the fact that the aorta was occluded at the level of the left subclavian artery or just distal to the left common carotid artery for periods up to one hour, none developed any evidence of cord damage.

As has been indicated above, our preliminary studies showed that in the dog occlusion of the major branches of the aortic arch is well tolerated, owing presumably to the presence of extensive collateral circulation. Even with the additional occlusion of the basilar artery only one of six animals

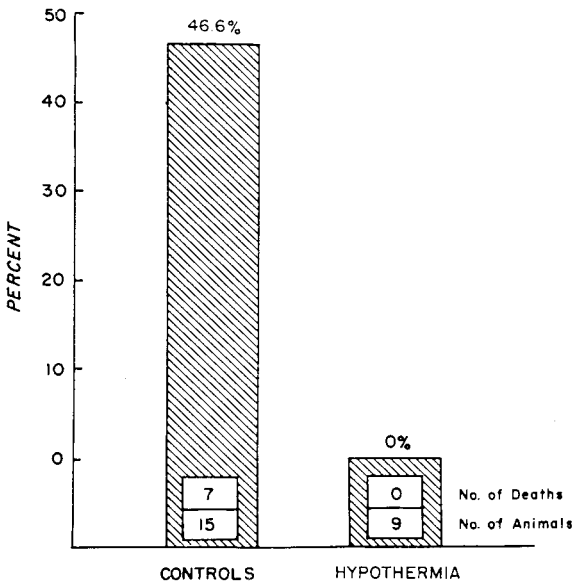

Fig. 2. Mortality in animals following temporary occlusion of cerebral circulation.

developed ischemic cerebral changes. Indeed, only after the occlusion of additional arterial pathways as was done in the group II experiments was it possible to reduce cerebral circulation sufficiently to produce an appreciable degree of ischemic damage. This was usually manifested by dilatation of the pupil in 3 to 9 minutes. Following restoration of cerebral blood flow the pupil may gradually decrease in size, but spontaneous respiration may not take place and death occurs upon termination of artificial respiration. In others while respiration may be resumed, the animal develops a state of tension responding to auditory and tactile stimuli with bursts of tonic convulsions and dying in a state of exhaustion within 6 to 24 hours.

Since none of these manifestations occurred in the comparable group of hypothermic animals it would appear that this procedure has a significant protective value in preventing ischemic damage to the brain in dogs following temporary arrest of cerebral circulation (Fig. 2). These observations conform with those recently reported by Parkins, Jensen and Vars,[8] who

found that brain cooling to 20° C. provides adequate protection against 30 minutes of complete circulatory occlusion. It would appear, therefore, that in the dog hypothermia has protective value in preventing ischemic brain damage following temporary arrest of the circulation. Accordingly it deserves further study as a promising means of overcoming this hazard in the clinical attack upon vascular lesions involving the major arterial channels to the brain.

SUMMARY

1. Studies were undertaken to determine the effectiveness of hypothermia in preventing brain damage following temporary arrest of the cerebral circulation. Following preliminary observations which revealed that in the dog temporary occlusion of the brachiocephalic, subclavian, carotid and vertebral arteries up to one hour produced no neurologic disturbance owing presumably to extensive collateral circulation, three groups of experiments were performed. In the first group the basilar artery was occluded and a tourniquet applied around the neck at a pressure of 900 mm. Hg for 30 minutes. In addition to this procedure in the second group, temporary occlusion of the carotid and vertebral arteries was done. The third group was similar to the second group except that the body temperature of these animals was reduced to about 25° to 31° C.

2. There was a striking increase in mortality from 16.7 per cent in the first group of animals to 66.6 per cent in the second group, indicating that the procedure in the latter group was much more effective in obstructing cerebral circulation. In the third group of animals in which the same experiment was done as in the second group except that hypothermia was used, there were no deaths and no other evidence of brain damage.

3. On the basis of these experiments it is concluded hypothermia appears to have protective value in the dog against ischemic damage to the brain following temporary arrest of cerebral circulation.

REFERENCES

1. Beattie, E. J., Jr., Adovasio, D., Keshishian, J. M., and Blades, B.: Refrigeration in experimental surgery of the aorta. Surg., Gynec. & Obst., *96*:711, 1953.
2. Bigelow, W. G., Lindsay, W. K., Harrison, R. C., Gordon, R. A., and Greenwood, W. F.: Oxygen transport and utilization in dogs at low body temperatures. Am. J. Physiol., *160*:125, 1950.
3. Cooley, D. A., and DeBakey, M. E.: Resection of the thoracic aorta with replacement by homograft for aneurysms and constrictive lesions. J. Thoracic Surg., 29:66–104, 1955.
4. DeBakey, M. E., and Cooley, D. A.: Successful resection of aneurysm of distal aortic arch and replacement by graft. J.A.M.A., *155*:1398, 1954.
5. Gardner, M. D.: Ligation of carotid and vertebral arteries in monkeys. Proc. Soc. Exp. Biol. & Med., *32*:1034, 1935.
6. Lam, C. R., and Aram, H. H.: Resection of descending thoracic aorta for aneurysm. Ann. Surg., *134*:743, 1951.
7. Martin, H., Del Valle, B., Ehrlich, H., and Cahan, W. G.: Neck dissection. Cancer, *4*:441–499, 1951.
8. Parkins, W. M., Jensen, J. M., and Vars, H. M.: Brain cooling in the prevention of brain damage during periods of circulatory occlusion in dogs. Ann. Surg., *140*: 284–289, 1954.
9. Pontius, R. G., Brockman, H. L., Hardy, E. G., Cooley, D. A., and DeBakey, M. E.: The use of hypothermia in the prevention of paraplegia following temporary aortic occlusion: experimental observations. Surgery, *36*:33–38, 1954.